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10/593,401	11/13/2006	Gerhard Muhrer	33696-US-PCT	2784
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NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 101/2 EAST HANOVER, NJ 07936-1080			EXAMINER HAGHIGHATIAN, MINA	
			ART UNIT 1616	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/593,401	<b>Applicant(s)</b> MUHRER ET AL.	
	<b>Examiner</b> Mina Haghighatian	<b>Art Unit</b> 1616	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 May 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-19 and 22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19, 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>04/10, 08/08, 09/06</u>                                       | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Election/Restrictions*

Receipt is acknowledged of the Election of Group I, claims 1-18 with traverse on 05/05/10. Applicant's arguments have been found persuasive, thus the election requirement filed on 04/08/10 is **withdrawn** and thus all pending claims, claims **1-19 and 22** will be examined on the merits.

### *Drawings*

The drawings are objected to because Figures **2 and 3** are not clear and would not be proper for printing and publication. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required

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corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim **19** is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 19 is drawn to the process according to claim 1, wherein said micronized pharmaceutically active agent is prepared in situ in an inhalation device.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a process for micronization of a pharmaceutically active agent by the steps of suspending the pharmaceutically active agent in a propellant or compressed gas and processing the suspension by high pressure

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homogenization to obtain dry powder upon depressurization, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim 19 is directed to encompass the said process taking place in situ in an inhalation device, which only correspond in some undefined way to specifically instantly disclosed process. Only the specifically disclosed process (of claim 1) meet the written description provision of 35 USC § 112, first paragraph. The process of preparing dry powder in situ in an inhalation device, however does not due to lacking details and information on how Applicants have accomplished the said process in situ in an inhalation device. Specification discloses that the said process is “for the industrial production of micron and submicron size particles of difficult-to-comminute pharmaceutically active agents” (see page 2, lines 3-6). It is also disclosed that the said process requires the step of high pressure homogenization. Specification describes the process as “may be efficiently controlled by closely controlling the characteristic process parameters of the proposed micronization process. Homogenization pressure, suspension density and solids concentration, operating temperature, choice of interaction geometries and number of passes through the equipment or combinations of theses main operating parameters may be used to closely control product quality” (see the paragraph bridging pages 6 and 7). As inhalation devices are simple and usually small handheld devices operated by patients, they are not capable of such process.

The specification provides no guidance to one of ordinary skill in the art on how such process is possible in situ in an inhalation device and thus does not fulfill the written description requirements.

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Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the process of claim 1 meet the written description provision of 35 USC § 112, first paragraph. The process of micronization in situ in an inhalation device does not. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Claims **1-19** are rejected under 35 U.S.C. 112, **first paragraph**, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendments of 05/05/10 limits the

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propellant component to a gas propellant. Specification does not recite a "gas propellant". Applicant provides no recite where there is support for the said amendment.

This is a new matter rejection.

The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 8 and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, 8 and 11-12 as written include the phrase "chosen from at least one of". Proper Markush language is "selected from the group consisting of". The examiner suggests rewording the claim to include the Markush language. **Note: MPEP 2111.03**

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeStefano et al (6,135,628).**

DeStefano et al teach a method and apparatus for homogenizing aerosol formulations. Disclosed is a method and apparatus for homogenizing and micronizing aerosol formulations. The method includes the steps of homogenizing and micronizing an aerosol formulation at ambient temperature in a closed apparatus where the entire apparatus is maintained under elevated pressure. The apparatus includes a closed loop containing a reaction vessel, a homogenizer and a fluid conduit interconnecting the reaction vessel and the homogenizer. The homogenizer includes an interaction chamber and an intensifier pump. The interaction chamber includes a stream splitter for

separating a stream of aerosol formulation components into two streams and an impaction chamber for recombining the stream (see abstract).

DeStephano et al teach a closed, pressurizable system for homogenizing aerosol formulations including the following components: (1) A pressurizable mixing vessel having inlet and outlet means; (2) A homogenizer disposed in fluid communication with the reaction vessel, said homogenizer including a plurality of nozzles having elongated orifices to eject under pressure sheets of the liquid to be homogenized, said nozzles being arranged to effect turbulent jet interaction of said sheets along a common jet interaction front and said sheets being ejected by said nozzles into a low-pressure zone filled with said liquid of the sheets along a common liquid jet interaction front and said sheets being ejected by said nozzles into a low-pressure zone filled with said liquid further creating turbulent jet interaction along a common boundary essentially defined and formed by said mixture in said low pressure zone and by said sheets ejected into said low pressure zone; jet interaction chamber-defining means arranged to provide said low pressure zone of said liquid system in which said turbulent jet interaction is effected; pump means for delivering said liquid system under pressure to said nozzles; and (3) fluid conduits running from said outlet of said mixing vessel to the homogenizer and from the homogenizer back to the inlet of the mixing vessel, to form a closed apparatus therebetween.

The present invention is also directed to a method for homogenizing an aerosol formulation in a closed continuous-loop system under elevated pressure, the method including the steps of determining a desired level of homogenization, mixing an aerosol

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formulation in a mixing vessel, circulating the mixed aerosol formulation through a high pressure homogenizer, operating the high pressure homogenizer at a pressure sufficient to achieve homogenization of the mixed aerosol formulation, circulating the aerosol formulation back into the mixing vessel and repeating the aforementioned steps until the desired level of homogenization is achieved.

The closed continuous loop system may be connected by connecting means and conduit means to a high pressure filling station to fill aerosol containers. In an alternative embodiment, the closed continuous loop system may be used to prepare a concentrated aerosol formulation which is transferred by connecting means and conduit means to a large vessel where it is diluted with the aerosol propellant to a predetermined volume of aerosol formulation. Accordingly, the objects of the disclosure are to provide: -an improved method and system for homogenizing volatile mixtures,

- a method and system for homogenizing volatile mixtures, such as aerosol formulations comprising low boiling HFA propellants, at ambient temperature,

- a method and system which permit the preparation of aerosol formulations comprising a wide range of surfactants, including those surfactants which would not be miscible in the formulation if processed at reduced temperature,

And to provide a method and system which can both micronize particles of active substance in an aerosol formulation and homogenize the formulation, eliminating the need for prior milling of the active substance (see col. 4, lines 9-35).

DeStefano et al also teach the device which includes a high pressure homogenizer 12 that operates upon an aerosol formulation at a pressure sufficient to

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achieve homogenization and, where applicable and desired, the simultaneous micronization of solid particles present in the aerosol formulation. The high pressure homogenizer 12 may be, for example, a Microfluidics Model M-110F Microfluidizer® (see col. 5, lines 22-65).

DeStefano et al teach that the active ingredient may include for example, a pharmaceutically effective amount of a pharmaceutically active respiratory compound. Active ingredients include, for example, ipratropium bromide and albuterol sulfate. Possible surfactants include, for example, perfluorocarboxylic acid, polyethyleneglycols, polyethylene oxide sorbitan fatty acid ester, sorbitan esters, such as sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate, and the like, polyvinylpyrrolidone, propylene glycol and oleic acid. A propellant is supplied to the reaction vessel 10, under pressure, through a valved inlet 11. The propellant may be, for example, a low boiling hydrocarbon; an HFA propellant such as HFA-227, HFA-134a or a combination of HFA-227 and HFA-134a; or a CFC propellant such as CFC 12 or 114, or a mixture thereof. The propellant may additionally comprise a solvent, such as for example an alcohol such as ethanol (see col. 6, lines 26-56).

DeStefano et al disclose that while carrying out the process of homogenization, or simultaneous homogenization and micronization, aerosol formulation flows through the components of the embodiment shown in FIG. 2 in the following sequence: starting from the mixing vessel 10, the formulation flows through the drain valve 50, conduit 30(c), the three-way valve 100, conduit 30(d), the high pressure homogenizer 12, the conduit 30(e), the three-way valve 101, conduit 30(f), the optionally present flow meter

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170, conduit 30(i), by-pass connector 110, open by-pass valve 90, conduit 30(n), the optionally present flow meter 171, conduit 30(o), and then back into the mixing vessel 10. Once homogenization and, if applicable, micronization is complete, the flow of formulation is diverted from the homogenizer 12, to the pump 70, by way of conduit 30(g) and conduit 30(h), by operation of the three-way valves 100 and 101. The high pressure homogenizer 12 is removed from the circulation path of the aerosol formulation to avoid over-processing of the aerosol formulation. Up to this point the pump of high pressure homogenizer 12 is responsible for the circulation of formulation through the apparatus. Once the flow of formulation is diverted from the high pressure homogenizer 12, the pump 70 takes over this task. The pump 70, as well as the stirrer 40 of the reaction vessel 10, impart sufficient agitation to maintain suspension. Preferably, after about 15 minutes of circulation by the pump 70, when both the temperature and the pressure within the vessel increase to values which are close to their starting values, dispensing may begin (see col. 9, lines 10-40).

While DeStefano et al does not anticipate the instant claims, it discloses every limitation and sufficient teachings to one of ordinary skill in the art to make and use the invention as claimed. DeStefano et al teach the process of micronization by way of high pressure homogenization while employing excipients such as surfactants to prepare suitable compositions for pulmonary delivery of active agents. “[w]hen an application simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an

arrangement, the combination is obvious". KSR v. Teleflex, 127 S.Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent application claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." Id. at 1742. Consistent with this reasoning, it would have been obvious to have selected specific steps and components of the prior art disclosure, to arrive at a process "yielding no more than one would expect from such an arrangement".

**Claims 1-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (6,228,346) in view of Bernini et al (WO 0025746).**

Zhang et al teach that propellant gases with a low evaporation enthalpy, such as carbon dioxide, sulfur hexafluoride and ethane, can be used in the subcritical state in a pharmaceutical aerosol, without entailing the aforementioned disadvantages, if they are mixed with another gas that has a high evaporation enthalpy and a low vapor pressure,

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such as butane, propane or dimethyl ether. The added gas has two functions: to decrease the overall system's vapor pressure and to increase the system's dissolving capacity. The system's evaporation enthalpy is still sufficiently small, with the result that problems do not arise during evaporation. Due to the presence of non-inflammable gas, the system's inflammability is also substantially reduced. A special propellant mixture is prepared for pharmaceutical aerosols so as to micronize the drugs for pulmonary application. This propellant mixture is present in the subcritical state and contains at least one component from a first class of propellant gases and at least one component from a second class of propellant gases, with different enthalpy and vapor pressures (see summary).

Zhnag et al teach a pharmaceutical aerosol for pulmonary application; in addition to one or more pharmaceutical substances, this aerosol contains: 1) a propellant mixture in an amount of from 10 to 80 wt. %, and wherein the pharmaceutical may be present in the aerosol composition in a dissolved state (solution aerosol) or in a suspended state (suspension aerosol); 2) A drug; 3) A surfactant which is frequently added in a suspension aerosol for enhanced suspension of the pharmaceutical. A suspension aerosol formulation requires the surfactant used to be soluble in the propellant mixture. The conventional surfactants, such as oleic acid, lecithin and sorbitan trioleate, are easily soluble in the 2nd propellant gas class and are also soluble in the propellant gas mixture used here. In consequence, such surfactants can be used without difficulty in the production of a suspension aerosol formulation.

The process produces particles generated by spraying, having a diameter of less than 8  $\mu\text{m}$ , and preferably, the particle size is less than 5  $\mu\text{m}$ . The percentages each relate to the total mass of the produced pharmaceutical particles "dried" after evaporating the propellant. These particles therefore have a smaller mass and are not so easily precipitated in the mouthpiece of the metered dose aerosol or in the spacer. Improved respirability means that not only the bronchial or upper pulmonary region, but also more deeply lying sections of the lungs and pulmonary alveoli are reached. This is not only a decisive advantage when the lung itself represents the affected organ to be treated, the resorption of systemic-action pharmaceuticals is also improved (see col. 4).

Zhang et al also teach that the compositions may contain other common, pharmaceutically compatible diluents, excipients, entrainers, solubilizers and surfactants. The pharmaceutical may be present in the aerosol composition as a solution or suspension with a percentage content of 0.01 to 5 wt. %, preferably 0.03 to 1 wt. %. The operating pressure of the composition is 2 to 100, preferably 3 to 50 bar, with particular preference for 5 to 20 bar. For micronization, a spray nozzle common for this purpose is used. In a preferred embodiment of the newly developed pharmaceutical aerosol, the propellant mixture solely comprises one or more components from the above two classes. The aforementioned solubilizers and/or surfactants can also be optionally present. To achieve specific or improved effects, a combination of different active ingredients with varying percentage contents can be used in an aerosol formulation, e.g. combinations of ipratropium bromide and fenoterol, salbutamol and

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disodium cromoglicinic acid, and salbutamol and beclometason-17,21-dipropionate (see col. 5).

Zhang et al teach a device that comprises a gas cylinder, a high-pressure pump, a safety valve, a check valve, a spray nozzle, and an autoclave. The high-pressure pump is used to pump dimethyl ether, propane or butane out of the cylinder, which is positioned on a balance, into the autoclave. The feed quantity can be read off from the balance. After the pressure in the autoclave has reached the desired value, it is agitated for about 90 minutes. It is then not moved for 30 minutes, causing all the undissolved substances to separate from the gas mixture. A high-pressure viewing cell with a 35 ml volume is used to evaluate the stability of a suspension. The viewing cell has a large viewing diameter of 30 mm, making it much easier to observe the suspension conventional nozzles are used to process aerosols (see col. 5, line 59 to col. 6. line 30). The suitable nozzle aperture of a spray nozzle depends on the operating pressure (see col. 8, lines 34-37). Process of preparing particles is also exemplified in Examples 1-9. Zhang et al discloses employing a high pressure pump in the process, but lacks specific disclosure on the step of high pressure homogenization. However, this deficiency is cured by Bernini et al.

Bernini et al a process for the preparation of suspensions of drug particles for inhalation delivery. The process includes the step of homogenising and micronising the formulation in a turboemulsifier provided with a high-potency turbine, optionally followed by a treatment in a high pressure homogenizer (see abstract). The high pressure

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homogenization reduces the mean size of the suspended particles. A typical apparatus used for this treatment, such as the Microfluidizer®, includes a high pressure pump which can supply pressures up to 1500 bar and one or more interaction chambers (see page 3, lines 12-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have implemented the step of high pressure homogenization of Bernini et al in the processes and formulations of Zhang et al with a reasonable expectation of successfully preparing dry powder particles in a suitable particle size with the known process of high pressure homogenization. In other words, the claims would have been obvious because the technique for improving a particular formulation was part of the ordinary capabilities of a person of ordinary skill in the art, in view of the teaching of the technique for improvement in other situations.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

**Claims 1-19 and 22 are rejected.**

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

Mina Haghighatian  
Primary Examiner  
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